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Monitoring the CD4 Count in HIV Patients under Anti-Retroviral Therapy (ART)

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ABSTRACT

Antiretroviral therapy (ART) is the recommended treatment for HIV patients. The CD4 count is an important parameter used to monitor the progression of HIV and critically regarding treatment decision. In the period between December 2012 and January 2015, blood samples were collected from 260 HIV patients attending the Central Lab of Ministry of Health, Two hundred patients were going on ART and sixty patients still without treatment, in addition to thirty normal persons used as a controller group. All were analyzed for CD4 count, comparing the two groups during 24 months of analysis. The CD4 count showed significant increase (p<0.0001) after ART. The results of this study clearly indicated that ART had been playing a role in CD4 maintenance and recovery enhancing the immune system and prove that the CD4 is the best indicator for following up HIV patients after ART adherence.

Key words: HIV patients, CD4 count, ART.

Introduction

The disease of HIV is transmitted by sexual contact, contaminated blood transfusions, infected needles and prenatal infection from mother to her new born or during breastfeeding (Mumtaz *et al.,* 2011).Despite a low prevalence of HIV, Egypt still faces several challenges in maintaining this low prevalence (Barakat and El Sayed, 2012).The virus of HIV attacks the immune system causing AIDS disease. Months to years after HIV infection and in absence of specific treatment as the illness progresses, the virus destroys most of T-cell lymphocytes. This disables the immune system to defend the body against diseases, tumors and various opportunistic infections will develop. The CD4 count is an important parameter used to monitor the progression of the virus and its effects on immune system. Also, CD4 monitoring remains a critical component for HIV care, to evaluate treatment efficacy and provide early warnings of treatment resistance or failure (Keiser *et al.,* 2011).

Antiretroviral therapy is the ideal treatment recommended for HIV infection; leads to rapid reduction in HIV RNA plasma levels and increase in peripheral CD4 cell count (Mocroft *et al.,* 2003). Early introduction of ART accompanied by dramatic reduction in morbidity and mortality associated with HIV infection (Baggaley *et al.,* 2008), and also reduce the complications such as tuberculosis (Abdel Aal *et al.,* 2013). Regimen of ART involves a combination of three or more anti-HIV medications daily, including two nucleoside reverse-transcriptase inhibitors plus non-nucleoside reverse-transcriptase inhibitor or protease inhibitor (Tebas*et al.,* 2013).

The present study aims to follow up the positive HIV patients, through monitoring the CD4 count in patients' adherent to (ART).

Materials and Methods

This prospective study, included 260 adult persons who attending the Voluntary Counseling and Testing unite (VCT) through the Central Laboratories of Ministry of Health, Cairo, Egypt, in the period between December 2012 and January 2015. Consent for participation was obtained. Cases involved both sexes, with age above 18 years. They divided into two groups; Two hundred patients started anti-retroviral therapy (group A), and sixty untreated patients (group B). Also, the study included thirty normal persons considered as a controller group (group C). As recommended by Zaaijer *et al.,*(1992) and Meier *et al.,*(1993), diagnosis of the HIV patients were done by fourth generation Enzyme Linked Immune Sorbent Assay (ELISA)using Enzygnost HIV Integral II Ab/Ag kits (Siemens, Germany),and confirmation the positivity of HIV by western blot techniques,

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being more specific and accurate for HIV using MP diagnostic kits(Germany)**.** The MP Diagnostics HIV BLOT 2.2 is a qualitative enzyme immunoassay for the in vitro detection of antibodies to HIV-I and HIV-II (Tsang *et al.,* 1985 and Ming Guan *et al.,* 2007). The CD4 count was monitored by flow cytometry method using FITC Mouse Anti-Human CD4 kits, through BDFACS Calibur full automated apparatus, every 3 months for 24 months (Knapp *et al.,* 1989 and Schlossman *et al.,* 1995).Genotyping detection of HIV RNA by Real Time PCR using Qiagen QIAamp viral RNA Mini Kits, as it enable rapid, efficient purification and concentration of high-quality viral nucleic acids, every 6 months (Lin *et al.,* 1997).

Total white blood cells& lymphocytic counts (for calculation of the CD4 count)and hemoglobin percentage(for changing the line of treatment in presence of anemia),the previous hematological tests were done using full automated cell counter (Sysmex) KXN-21 system (Japan) & Stromatolyser WH kits. The system provides a high level of accuracy through the use of automatic floating discriminators.

Results

The present study showed, statistical significant difference between patients maintained on treatment (Group A) and patients without treatment (Group B) regarding the CD4 count and total lymphocytic count, through 24 months. The CD4 count and its percentage changes were performed to all positive HIV patients, in comparison to the first reading (base line), every three months for nine readings.

In group A (under ART), it was found that, the mean CD4 count was 54.412, which is highly significant increase (p<0.0001), and there was 98% increase of the CD4 count in the last reading compared to first one.

However, in group B (without treatment), the mean CD4 count was about 40.255 which is highly significant decrease (p<0.0001). Also there was 73% decrease in the CD4 count comparing first reading to the last one.

This study revealed that, 48 (24%) patients out of 200 in group A had CD4 count more than 350 cells/ mm^3. After 24 months of ART, numbers of patients with CD4 count >350 increased to become 141(71%). In contrast, after 24 months without treatment in Group B, 34 patients (57%) out of 60, reduced to zero patients (0 %)with CD4 count more than 350 cells/ mm^3 (Table 3).

Table 1: Monitoring changes in CD4 count & its percentage compared to 1st reading among group A (Every 3 months of ART)

Every 3 months	1st Reading	2nd Reading	3rd Reading	4th Reading	5th Reading	6th Reading	7th Reading	8th Reading	9th Reading	PF
Mean ± SD	240.7 ± 134.0	303.7 ± 138.4	322.2 ± 153.4	370.5 ± 160.7	397.7 ± 172.3	423.2 ± 166.3	453.0 ± 171.9	465.5 ± 156.4	477.2 ± 143.2	<0.0001 54.412
Mean change compared to 1st reading in %		26%	34%	54%	65%	76%	88%	93%	98%	%

**p value<0.001(highly significant, *p value>0.05 (non-significant)*

Table 2: Monitoring changes in CD4 count & its percentage compared to 1st reading among group B(Every 3 months without ART)

Every 3 months	1st Reading	2nd Reading	3rd Reading	4th Reading	5th Reading	6th Reading	7th Reading	8th Reading	9th Reading	PF
Mean ± SD	357.8 ± 109.4	288.9 ± 140.1	218.5 ± 145.9	164.2 ± 144.3	145.5 ± 114.6	115.7 ± 97.14	111.0 ± 86.13	101.2 ± 71.2	98 ± 74.6	<0.0001 40.255
Mean change compared to 1st reading in %		-19%	-39%	-54%	-59%	-68%	-69%	-71%	-73%	%

**p value<0.001(highly significant, *p value>0.05 (non-significant)*

Table 3: Changes in CD4 count in treated & untreated groups (A & B) after 24 months of analysis

Number of patients included in groups A&B	CD4 Count analysis	
	At the start of analysis	After 24 months of analysis
	> 350 cells/ mm^3	> 350 cells/ mm^3
Treated group A (200) patients	48 (24%)	141 (71%)
Untreated group B (60) patients	34 (57%)	zero (0%)

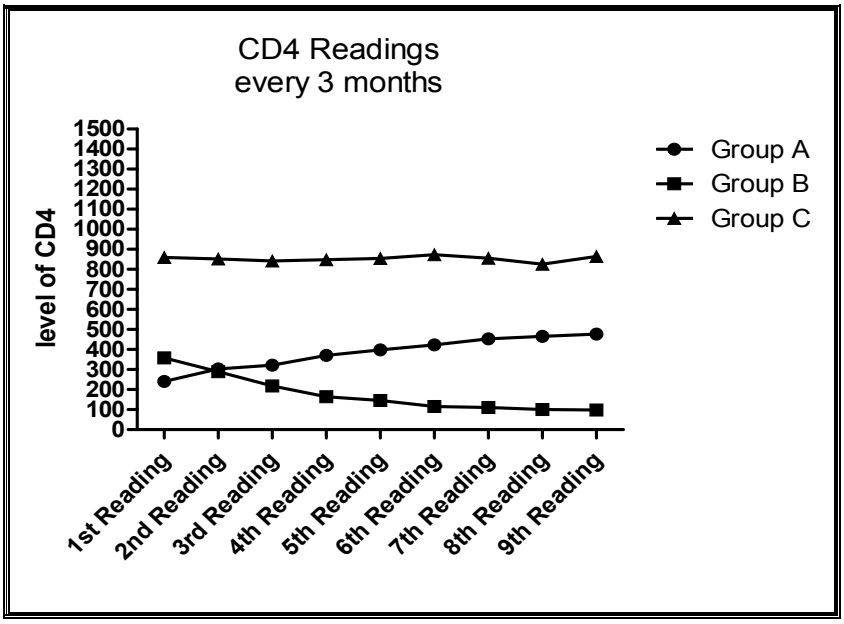

Fig. 1: Changes in CD4 count among all groups (Through 24 months, 3 months interval)

Discussion

In treated group A, there was an increase in CD4 count by 98% compared to the level before starting treatment (base line reading). On another hand in untreated group B, there was a decrease in CD4 count by-73% compared to first reading. This is in agreement with the studies of Petoumenos *et al*. (2015) and Saison *et al*. (2015), which reported an elevation in the level of CD4 count in patients started ART earlier than patients did not adherent to ART or delayed treatment. Also, our study is in accordance with the studies obtained by Kitahata *et al*. (2009) and Tuan *et al*. (2013), where there were an increase in the CD4 count of HIV infected patients maintained on antiretroviral therapy.

In group A, the results obtained showed, an increase in the number of patients from 48 patients to 141 patients having CD4 count more than350 cells/ mm^3 after 24 months of treatment. In contrary, in untreated group B, the number of patients decreased from 36 to zero patients having CD4 more than 350 cells/ mm^3after 24 months without treatment. This is in accordance with the studies done by Cain *et al*. (2011) and Doshi *et al*.(2012), which showed that the HIV-positive patients who started antiretroviral therapy and possessed CD4 count between 350 - 550 cells/ mm^3or more, gain much CD4 count higher than patients whom started ART with relatively lowerCD4 count especially below 250 cells/ mm^3.

Patients in group A, who started treatment with CD4 counts more than 350 cells/ mm^3 associated with low viral load, had a significant increase in CD4 counts and decrease in viral load reaching to undetectable level (with a probability of virological success / free) after 24 months of ART, than patients who started treatment with CD4 count less than 350 cells/ mm^3 and high viral load in the same treated group. These results had a great similarity with the studies obtained by Kitahata *et al*. (2009)and Jason *et al*.(2012).Where through the 2 years course of treatment, the patients starting ART with CD4 count $\geq$ 350cells/ mm^3 and low viral load had no virologic failure. However, there were one or more virologic failure in patients starting ART withCD4 $\leq$ 350 cells/mm^3 and high viral load, after 6 - 9 months of treatment. Also, the CD4 counts in people who started with the lowest counts did not catch up the CD4 count in people who started with higher count (Hughes *et al.,* 2011). Virologic failure with high viral load had a greater negative impact on CD4 cell gain (Sterne *et al.,* 2009).

Conclusion

Antiretroviral therapy has been playing a role in maintenance of CD4 cell count in HIV infected patients. The success of ART depends on monitoring the effectiveness of ART at a right time through monitoring the CD4& viral load between 3-6 months.

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